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(54) Title: SMALL PEPTIDES CAPABLE OF MODULATING THE FUNCTION OF CD66 (CEACAM) FAMILY MEMBERS

(57) Abstract: The present invention relates to peptides capable of modulating the function (e.g., signaling or adhesive activities) of CD66 (CEACAM) family members and/or their ligands.

SMALL PEPTIDES CAPABLE OF MODULATING THE FUNCTION OF CD66 (CEACAM) FAMILY MEMBERS

BACKGROUND OF THE INVENTION

CD66 family members appear to play a role in a wide variety of normal and pathological processes, including: cancer, embryonic development, bacterial infection, viral infection, inflammation, pregnancy, bile transport, and cell adhesion (1-3). CD66 monoclonal antibodies (mAbs) react with members of the carcinoembryonic antigen (CEA) family (4-13). In the CD terminology, mAbs belonging to the CD66 cluster are classified according to their reactivity with each family member, as indicated by a lower case letter after "CD66" as follows: CD66a, CEACAM-1 or biliary glycoprotein (BGP); CD66b, CEACAM-8 or CGM6; CD66c, CEACAM-6 or NCA; CD66d, CEACAM-3 or CGM1; CD66e, CEA; and CD66f, pregnancy specific glycoprotein (PSG) (13, 14). The CD66 (CEA) gene family belongs to the immunoglobulin (Ig) gene superfamily [for review see (1, 2, 15). Structurally, each of the human CD66 family members contains one amino-terminal (N) domain of 108-110 amino acid residues, homologous to Ig variable domains, followed by a differing number (0-6) of Ig C2-type constant-like domains. The structure of the N-domain is therefore predicted to be a stacked pair of beta-sheets with 9 beta-strands (16).

CD66 family members may potentially function as adhesion molecules (12, 17-30). CD66a, CD66c, and CD66e are capable of homotypic and heterotypic adhesion, as shown by use of recombinant CD66a which undergoes homotypic adhesion as well as heterotypic adhesion with CD66c and CD66e (1, 2, 4-12, 17-32). Data also suggest that CD66a plays a signaling role and regulates the adhesion activity of CD11/CD18 in human neutrophils (8, 11, 25-27, 33, 34). CD66a, CD66b, CD66c, and CD66d, but not CD66e, are expressed in human neutrophils, where they are "activation antigens" in that their surface

expression is increased following neutrophil stimulation with various stimuli. CD66a, CD66b, CD66c, and CD66d mAb binding to the neutrophil surface triggers a transient activation signal that regulates the adhesive activity of CD11/CD18, and increases neutrophil adhesion to human umbilical vein endothelial cells (HUVECs) (8, 11, 25-27, 33, 34).

CD66a is frequently down regulated in colon, prostate, breast, and hepatocellular carcinoma, and colorectal adenomas (35-39). Transfection studies have provided evidence that CD66a may act as a tumor suppressor in models of colon cancer (40) prostate cancer (41, 42) breast cancer (43) and bladder cancer (44). CD66a is also important in bacterial infections, since over 95% of pathogenic N. meningitidis and N. gonorrhea interact with CD66a via Opa proteins, and the binding site for these Opa proteins has been localized to the N-domain of CD66a (45-50). An important property of Opa proteins is the stimulation of adhesion and non opsonic phagocytosis of Opa+ bacteria by neutrophils (reviewed in 48). CD66a also appears to function as a receptor for murine hepatitis virus (51-55). Furthermore, CD66a may play a role in angiogenesis since it is selectively expressed on certain endothelial cells (56) and CD66a appears to function as a regulator of bile transport in bile canaliculi (3, 57, 58).

The mechanism(s) by which CD66a transmits signals (e.g. activation in neutrophils, or growth regulating signals in epithelial cells and carcinomas) are unclear. However, CD66a is phosphorylated on its cytoplasmic domain, largely on tyrosine with a lower level of phosphoserine, in neutrophils and colon cancer cells (4, 59-61). While at least eight isoforms of CD66a derived from differential splicing have been described (3, 12, 13, 25), only those isoforms with a long cytoplasmic tail can be phosphorylated on tyrosine. In addition, associated protein tyrosine kinase and phosphatase activities may be involved in CD66a signaling (59, 62, 63).

SUMMARY OF INVENTION

The present invention relates to peptides capable of modulating the function (e.g., signaling or adhesive activities) of CD66 (CEACAM) family members and/or their ligands. Active peptides (i.e., those capable of modulating the function of at least one CD66 family member and/or at least one ligand thereof) could be larger or smaller than the ones described here. While the present peptides described are of about 2-14 amino acids, peptides containing a relatively large number of amino acid residues, e.g., up to about 100 amino acid residues or more, that contain the described peptides, portions thereof, or similar peptides may have biological activity as well. Similarly, peptides with amino acid substitutions or other alterations may block the activities of the described peptides or the parent molecules. Cyclic or otherwise modified forms of the peptides would also be expected to have biological activity.

The present peptides may be, but are not limited to, peptides synthesized from regions of CD66 family members predicted to be exposed on the surface of the molecule. The present peptides are preferably capable of altering signaling mediated in part by CD66 (CEACAM) family members. Preferably, the peptides of the present invention modulate at least one of the following (which are functions of CD66 proteins and/or ligands thereof): activation of neutrophils; activation or inhibition of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of epithelial cells such as breast or intestinal/colonic epithelium cells or keratinocytes. In addition these peptides are preferably capable of altering homotypic and/or heterotypic adhesion among CD66 proteins (i.e., CD66 family members) or adhesion of CD66 proteins to other CD66 ligands.

Thus, the present invention provides isolated peptides or analogs thereof that modulate the function of at least one CD66 protein (i.e., CD66 family member) and/or at least one ligand thereof. These amino acid sequences can

form a part of a larger peptide. Additionally, they can be used in various combinations in any one peptide. Preferably, the present invention provides isolated peptides shown in the attached Tables I-XVII, including isolated peptides having an amino acids sequences of SEQ ID NO:2-111, 135-861 or TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG. It is believed they would have activity if they were solubilized or conjugated in a complex.

The present invention also provides peptide conjugates. The ability of peptides complexed with carrier molecules or structures, such as microbeads, liposomes, biological carrier molecules, synthetic polymers, biomaterials, and cells, thereby forming peptide conjugates is shown to impart the larger structure with the ability to bind to cells expressing the appropriate CD66 family

member. Such peptide conjugates bind to cells expressing a CD66 protein or a CD66 ligand.

The peptides or peptide conjugates of the present invention can also include molecules for labeling (i.e., labels such as fluroescence tags, magnetic resonance tags, radioactive tags, enzymatic tags). In this way, these can be used in diagnostic methods to detect specific targets *in vivo* or *in vitro*.

The present invention provides a method of activating a neutrophil that includes contacting the neutrophil with a peptide or peptide conjugate (i.e., at least one peptide or peptide conjugate) that includes an amino acid sequence shown in the attached Tables I-XVII or analogs thereof.

The present invention also provides a method of modulating the homotypic and/or heterotypic adhesion of CD66 family members or adhesion of a CD66 protein to a CD66 ligand. The method includes contacting CD66 family members and/or their ligands with a peptide or peptide conjugate that includes an amino acid shown in the attached Tables I-XVII or analogs thereof.

The present invention also provides a method of modulating (e.g., activating or inhibiting) immune cell (e.g., T-cells, B-cells, NK cells, LAK cells, or dendritic cells) activation, proliferation, and/or differentiation that includes contacting an immune cell with a peptide or peptide conjugate that includes an amino acid sequence shown in the attached Tables I-XVII or analogs thereof.

In addition, some peptides differ from these peptides by one or several amino acids and could compete with these active peptides or the natural CD66 family member or ligand thereof for certain biological activities.

For example, the present invention provides a method of blocking the activation of a neutrophil induced by the method described above. This method includes contacting the neutrophil when in the presence of at least one of the peptides used in the method of activating a neutrophil discussed above with at least one peptide or peptide conjugate that includes an amino acid sequence shown in the attached Tables I-XVII or analogs thereof.

As another example, the present invention provides a method of altering the modulation of the homotypic and/or heterotypic adhesion of CD66 family

members or adhesion between a CD66 protein and a CD66 ligand induced by peptides homologous to (e.g., peptides derived from similar regions of similar domains of CD66 family members) those listed in attached Tables I-XVII or analogs thereof. The method includes contacting CD66 family members and/or ligands thereof with a peptide comprising an amino acid sequence shown in the attached Tables I-XVII, or analogs thereof, when in the presence of at least one of the peptides listed above. This modulating effect can result, for example from direct binding of one of these peptides to one of the CD66 family members and/or ligands thereof, or from altering the effects of other peptides on the adhesion.

Another method of the present invention involves modulating at least one of the following functions of CD66 family members and/or ligands thereof in cells: activation of neutrophils; activation or inhibition of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of T-cells, B-cells, LAK cells, NK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of epithelial cells; homotypic and/or heterotypic adhesion among CD66 family members; and adhesion of CD66 family members to other ligands. The method includes contacting cells with at least one peptide or peptide conjugate that includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof.

Another method involves delivering a therapeutically active agent to a patient. The method includes administering at least one peptide conjugate comprising a peptide and the therapeutically active agent to a patient wherein the peptide includes an amino acid shown in attached Tables I-XVII or analogs thereof. Preferably, the therapeutically active agent is selected from drugs, DNA sequences, RNA sequences, proteins, lipids, and combinations thereof. More preferably, the therapeutically active agent is an antibacterial agent, antiinflammatory agent, or antineoplastic agent.

There is also provided a method of modifying the metastasis of malignant cells. This method includes contacting the malignant cells or normal host tissue with at least one peptide or peptide conjugate that includes an amino acid sequence shown in the attached Tables I-XVII, or analogs thereof.

There is also provided a method of altering bacterial or viral binding to cells or a biomaterial. The method includes contacting the cells or biomaterial with at least one peptide or peptide conjugate that includes an amino acid sequence shown in the attached Tables I-XVII, or analogs thereof.

Another method involves altering cell adhesion to a biomaterial. The method includes contacting the biomaterial with at least one peptide or peptide conjugate that includes an amino acid shown in the attached Tables I-XVII, or analogs thereof.

Another method involves detecting tumors. The method includes contacting tumor cells or tumor vasculature with at least one peptide or peptide conjugate that includes an amino acid shown in attached Tables I-XVII, or analogs thereof.

Still another method involves detecting inflammation. The method includes contacting inflamed vasculature or leukocytes with at least one peptide or peptide conjugate that includes an amino acid shown in attached Tables I-XVII, or analogs thereof.

Yet another method involves detecting a CD66 protein or a ligand thereof. The method includes contacting tissue containing a CD66 protein or a ligand thereof with at least one peptide or peptide conjugate that includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof.

Another method involves altering angiogenesis. The method includes contacting endothelial cells, tumor cells, or immune cells with at least one peptide or peptide conjugate that includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof.

Yet another method of the present invention involves altering an immune response. The method includes contacting immune system cells with at least one peptide or peptide conjugate that includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof.

Another method of the present invention involves altering keratinocyte proliferation. The method includes contacting keratinocytes with at least one peptide or peptide conjugate that includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof.

The methods described herein can be carried out *in vitro* or *in vivo*. The peptides can be used alone or in various combinations as well as in peptide conjugates. They are used in amounts that provide the desired effect. These amounts can be readily determined by one of skill in the art. Preferably, for each of the methods of the present invention, useful peptides are shown in attached Tables I-XVII, or analogs thereof.

As used herein, "a" or "an" refers to one or more of the term modified. Thus, the compositions and methods of the present invention include one or more polypeptides. Also, herein when peptide is said to includes an amino acid sequence shown in attached Tables I-XVII, or analogs thereof, the peptide can include one or more of the sequences specified.

"Amino acid" is used herein to refer to a chemical compound with the general formula: NH_2-CRH-COOH, where R, the side chain, is H or an organic group. Where R is an organic group, R can vary and is either polar or nonpolar (i.e., hydrophobic). The amino acids of this invention can be naturally occurring or synthetic (often referred to as nonproteinogenic). As used herein, an organic group is a hydrocarbon group that is classified as an aliphatic group, a cyclic group or combination of aliphatic and cyclic groups. The term "aliphatic group" means a saturated or unsaturated linear or branched hydrocarbon group. This term is used to encompass alkyl, alkenyl, and alkynyl groups, for example. The term "cyclic group" means a closed ring hydrocarbon group that is classified as an alicyclic group, aromatic group, or heterocyclic group. The term "alicyclic group" means a cyclic hydrocarbon group having properties resembling those of aliphatic groups. The term "aromatic group" refers to mono- or polycyclic aromatic hydrocarbon groups. As used herein, an organic group can be substituted or unsubstituted.

The terms "polypeptide" and "peptide" as used herein, are used interchangeably and refer to a polymer of amino acids. These terms do not connote a specific length of a polymer of amino acids. Thus, for example, the terms oligopeptide, protein, and enzyme are included within the definition of polypeptide or peptide, whether produced using recombinant techniques, chemical or enzymatic synthesis, or naturally occurring. This term also

includes polypeptides that have been modified or derivatized, such as by glycosylation, acetylation, phosphorylation, and the like.

Herein, "isolated" as it refers to peptides (i.e., polypeptides) means that the peptides are derived from naturally occurring proteins or other polypeptides and free from other biological material or they are synthesized, either recombinantly or chemically.

We have previously reported several peptides (14 amino acids in length) derived from CD66 (CEACAM) family members that have biological activity. We here demonstrate that smaller fragments of these peptides have biological activity further substantiating our previous claims that such is the case. The peptides of the present invention may be two amino acids in length, more preferably three amino acids in length and most preferably four or more amino acids in length.

The following abbreviations are used throughout the application:

A = Ala = Alanine	T = Thr = Threonine
V = Val = Valine	C = Cys = Cysteine
L = Leu = Leucine	Y = Tyr = Tyrosine
I = Ile = Isoleucine	N = Asn = Asparagine
P = Pro = Proline	Q = Gln = Glutamine
F = Phe = Phenylalanine	D = Asp = Aspartic Acid
W = Trp = Tryptophan	E = Glu = Glutamic Acid
M = Met = Methionine	K = Lys = Lysine
G = Gly = Glycine	R = Arg = Arginine
S = Ser = Serine	H = His = Histidine

Table I: Scrambled versions of Peptide S28 (CD66a-24)

Peptide Name	Amino Acid Sequence	SEQ ID NO:
S28 (CD66a-24)	TNDTGISIRWFFKN	1
S159	GIWRFSKDFTINTN	2
S160	KIDNFTSNGFTIWR	3

Table II: Smaller Parts of Peptide S28 (CD66a-24)

Peptide Name	Amino Acid Sequence	Location in Peptide S28	SEQ ID NO:
S180	TNDTGIS	Left	4
S181	TGISIRW	Middle	5
S182	IRWFFKN	Right	6

Table III: Smaller Parts of Peptide S28 (CD66a-24)*

Number of Amino Acids	Amino Acid Sequence	SEQ ID NO:
13	NDTGISIRWFFKN	7
13	TNDTGISIRWFFK	8
12	TNDTGISIRWFF	9
12	NDTGISIRWFFK	10
12	DTGISIRWFFKN	11
11	TNDTGISIRWF	12
11	NDTGISIRWFF	13
11	DTGISIRWFFK	14
11	TGISIRWFFKN	15
10	TNDTGISIRW	16
10	NDTGISIRWF	17
10	DTGISIRWFF	18
10	TGISIRWFFK	19
10	GISIRWFFKN	20
9	TNDTGISIR	21
9	NDTGISIRW	22
9	DTGISIRWF	23
9	TGISIRWFF	24
9	GISIRWFFK	25
9	ISIRWFFKN	26
8	TNDTGISI	27
8	NDTGISIR	28
8	DTGISIRW	29
8	TGISIRWF	30
8	GISIRWFF	31
8	ISIRWFFK	32
8	SIRWFFKN	33
7	TNDTGIS	4
7	NDTGISI	34
7	DTGISIR	35
7	TGISIRW	5
7	GISIRWF	36
7	ISIRWFF	37
7	SIRWFFK	38

7	IRWFFKN	6
6	TNDTGI	39
6	NDTGIS	40
6	DTGISI	41
6	TGISIR	42
6	GISIRW	43
6	ISIRWF	44
6	SIRWFF	45
6	IRWFFK	46
6	RWFFKN	47
5	TNDTG	48
5	NDTGI	49
5	DTGIS	50
5	TGISI	51
5	GISIR	52
5	ISIRW	53
5	SIRWF	54
5	IRWFF	55
5	RWFFK	56
5	WFFKN	57
4	TNDT	58
4	NDTG	59
4	DTGI	60
4	TGIS	61
4	GISI	62
4	ISIR	63
4	SIRW	64
4	IRWF	65
4	RWFF	66
4	WFFK	67
4	FFKN	68
3	TND	
3	NDT	
3	DTG	
3	TGI	
3	GIS	
3	ISI	
3	SIR	
3	IRW	
3	RWF	
3	WFF	

3	FFK	
3	FKN	
2	TN	
2	ND	
2	DT	
2	TG	
2	GI	
2	IS	
2	SI	
2	IR	
2	RW	
2	WF	
2	FF	
2	FK	
2	KN	

*S28 represents the amino acid sequence TNDTGISIRWFFKN (SEQ ID NO:1). This peptide was described in the International Patent Application Serial No. PCT/US00/23482 (filed August 26, 2000) as CD66a-24.

Table IV: Analogs of Peptide S28 (CD66a-24) with Naturally Occurring Amino Acids Added onto the Amino or Carboxy Terminus*

Amino Acid Sequence	SEQ ID NO:
STN	
STND	69
STNDT	70
STNDTG	71
STNDTGI	72
CSTN	73
CSTND	74
CSTNDT	75
CSTNDTG	76
CSTNDTGI	77
TCSTN	78
TCSTND	79
TCSTNDT	80
TCSTNDTG	81
TCSTNDTGI	82
LTCSTN	83
LTCSTND	84

LTCSTNDT	85
LTCSTNDTG	86
LTCSTNDTGI	87
KNQ	
FKNQ	88
FFKNQ	89
WFFKNQ	90
RWFFKNQ	91
KNQS	92
FKNQS	93
FFKNQS	94
WFFKNQS	95
RWFFKNQS	96
KNQSL	97
FKNQSL	98
FFKNQSL	99
WFFKNQSL	100
RWFFKNQSL	101
KNQSLP	102
FKNQSLP	103
FFKNQSLP	104
WFFKNQSLP	105
RWFFKNQSLP	106
KNQSLPS	107
FKNQSLPS	108
FFKNQSLPS	109
WFFKNQSLPS	110
RWFFKNQSLPS	111

*Since subfragments of peptide S28 exhibit activity (see Fig. 3), it is possible that any fragment of S28 may have biological activity. Also, adding additional amino acids to the sequences listed in Table III would generate peptides that would be expected to have activity as well.

Therefore, the invention includes any of the peptides listed in Table III with additional amino acids (sequences from the native protein or other sequences) attached.

For example, including but not limited to those listed above in Table IV.

Table V: CD66 Peptides from which Smaller Parts or Analogs Could be Generated*

Peptide Name	Additional Table**	Amino Acid Sequence	SEQ ID NO:
CD66a-1	X	SMPFNVAEGKEVL	112
CD66a-2	X	LVHNLPQQLFGYSW	113
CD66a-3	X	KGERVDGNRQIVGY	114
CD66a-7 = CD66c-7, CD66d-7, CD66e-7	X	VIKSDLVNEEATGQ	115
CD66a-15 = CD66b-15 = CD66c-15	X	SDPVTLNVTYGPDT	116
CD66a-16		PSDTYYRPGANLSL	117
CD66a-17		AASNPPAQYSWLIN	118
CD66a-18		LINGTFQQSTQELF	119
CD66a-19 = CD66e-21	X	FIPNITVNNSGSYT	120
CD66a-21		TTVKTIIVTELSPV	121
CD66a-23		SKTTVTGDKDSVNL	122
CD66a-26		ERMKLSQGNTTLSI	123
CD66a-6L = CD66c-6L	X	TIYPNASLLIQNVT	124
CD66b-10		PETQNTTYLWWVNG	125
CD66c-10		PEVQNTTYLWWVNG	126
CD66c-12		LQLSNGNMTLTLLS	127
CD66c-17		AASNPPAQYSWFIN	128
CD66c-19		IPNITVNNSGSYM	129
CD66e-2 = CD66d-2	X	LVHNLPQHLFGYSW	130
CD66e-3	X	KGERVDGNRQIIGY	131
CD66e-19	X	AASNPPAQYSWFVN	132
CD66e-31	X	SVDHSDPVILNVLY	133
CD66e-42	X	PEAQNTTYLWWVNG	134

*Smaller parts of the functionally active CD66 peptides that were previously described [International Patent Application Serial No. PCT/US00/23482 (filed August 26, 2000)] would have activity. Smaller parts would be generated in the same manner as shown in Table III for peptide S28. In addition, analogs of these peptides would be generated in the same manner as shown in Table IV for peptide S28.

**As further examples, for these peptides, smaller versions have been generated, as shown in the following tables. Similar smaller versions of the peptides without an "X" could be generated based on these examples.

Table VI: Short parts of Peptide CD66a-1 = SMPFNVAEGKEVL

Amino Acid Sequence	SEQ ID NO:
SMPFNVAEGKEV	135
MPFNVAEGKEVL	136
SMPFNVAEGKE	137
PFNVAEGKEVL	138
MPFNVAEGKEV	139
SMPFNVAEGK	140
MPFNVAEGKE	141
PFNVAEGKEV	142
FNVAEGKEVL	143
SMPFNVAEG	144
MPFNVAEGK	145
PFNVAEGKE	146
FNVAEGKEV	147
NVAEGKEVL	148
SMPFNVAE	149
MPFNVAEG	150
PFNVAEGK	151
FNVAEGKE	152
NVAEGKEV	153
VAEGKEVL	154
SMPFNVA	155
MPFNVAE	156
PFNVAEG	157
FNVAEGK	158
NVAEGKE	159
VAEGKEV	160
AEGKEVL	161
SMPFNV	162
MPFNVA	163
PFNVAE	164
FNVAEG	165
NVAEGK	166

VAEGKE	167
AEGKEV	168
EGKEVL	169
SMPFN	170
MPFNV	171
PFNVA	172
FNVAE	173
NVAEG	174
VAEGK	175
AEGKE	176
EGKEV	177
GKEVL	178
SMPF	179
MPFN	180
PFNV	181
FNVA	182
NVAE	183
VAEG	184
AEGK	185
EGKE	186
GKEV	187
KEVL	188
SMP	
MPF	
PFN	
FNV	
NVA	
VAE	
AEG	
EGK	
GKE	
KEV	
EVL	
SM	
MP	
PF	
FN	
NV	
VA	
AE	
EG	

GK	
KE	
EV	
VL	

Table VII: Short parts of Peptide CD66a-2 = LVHNLPQQLFGYSW

Amino Acid Sequence	SEQ ID NO:
LVHNLPQQLFGYSW	113
LVHNLPQQLFGYS	189
VHNLPQQLFGYSW	190
LVHNLPQQLFGY	191
VHNLPQQLFGYS	192
HNLPQQLFGYSW	193
LVHNLPQQLFG	194
VHNLPQQLFGY	195
HNLPQQLFGYS	196
NLPQQLFGYSW	197
LVHNLPQQLF	198
VHNLPQQLFG	199
HNLPQQLFGY	200
NLPQQLFGYS	201
LPQQLFGYSW	202
LVHNLPQQL	203
VHNLPQQLF	204
HNLPQQLFG	205
NLPQQLFGY	206
LPQQLFGYS	207
PQQLFGYSW	208
LVHNLPQQ	209
VHNLPQQL	210
HNLPQQLF	211
NLPQQLFG	212
LPQQLFGY	213
PQQLFGYS	214
QQLFGYSW	215
LVHNLPQ	216

VHNLPQQ	217
HNLPQQL	218
NLPQQLF	219
LPQQLFG	220
PQQLFGY	221
QQLFGYS	222
QLFGYSW	223
LVHNLP	224
VHNLPQ	225
HNLPQQ	226
NLPQQL	227
LPQQLF	228
PQQLFG	229
QQLFGY	230
QLFGYS	231
LFGYSW	232
LVHNL	233
VHNLP	234
HNLPQ	235
NLPQQ	236
LPQQL	237
PQQLF	238
QQLFG	239
QLFGY	240
LFGYS	241
FGYSW	242
LVHN	243
VHNL	244
HNLP	245
NLPQ	246
LPQQ	247
PQQL	248
QQLF	249
QLFG	250
LFGY	251
FGYS	252
GYSW	253
LVH	
VHN	
HNL	
NLP	

LPQ	
PQQ	
QQL	
QLF	
LFG	
FGY	
GYS	
YSW	
LV	
VH	
HN	
NL	
LP	
PQ	
QQ	
QL	
LF	
FG	
GY	
YS	
SW	

Table VIII: Short parts of Peptide CD66a-3 = KGERVDGNRQIVGY

Amino Acid Sequence	SEQ ID NO:
KGERVDGNRQIVGY	114
KGERVDGNRQIVG	254
GERVDGNRQIVGY	255
KGERVDGNRQIV	256
GERVDGNRQIVG	257
ERVDGNRQIVGY	258
KGERVDGNRQI	259
GERVDGNRQIV	260
ERVDGNRQIVG	261
RVDGNRQIVGY	262
KGERVDGNRQ	263
GERVDGNRQI	264
ERVDGNRQIV	265

RVDGNRQIVG	266
VDGNRQIVGY	267
KGERVDGNR	268
GERVDGNRQ	269
ERVDGNRQI	270
RVDGNRQIV	271
VDGNRQIVG	272
DGNRQIVGY	273
KGERVDGN	274
GERVDGNR	275
ERVDGNRQ	276
RVDGNRQI	277
VDGNRQIV	278
DGNRQIVG	279
GNRQIVGY	280
KGERVDG	281
GERVDGN	282
ERVDGNR	283
RVDGNRQ	284
VDGNRQI	285
DGNRQIV	286
GNRQIVG	287
NRQIVGY	288
KGERVD	289
GERVDG	290
ERVDGN	291
RVDGNR	292
VDGNRQ	293
DGNRQI	294
GNRQIV	295
NRQIVG	296
RQIVGY	297
KGERV	298
GERVD	299
ERVDG	300
RVDGN	301
VDGNR	302
DGNRQ	303
GNRQI	304
NRQIV	305

RQIVG	306
QIVGY	307
KGER	308
GERV	309
ERVD	310
RVDG	311
VDGN	312
DGNR	313
GNRQ	314
NRQI	315
RQIV	316
QIVG	317
IVGY	318
KGE	
GER	
ERV	
RVD	
VDG	
DGN	
GNR	
NRQ	
RQI	
QIV	
IVG	
VGY	
KG	
GE	
ER	
RV	
VD	
DG	
GN	
NR	
RQ	
QI	
IV	
VG	

Table IX: Short parts of Peptide CD66a-7 = VIKSDLVNEEATGQ

Amino Acid Sequence	SEQ ID NO:
VIKSDLVNEEATGQ	115
VIKSDLVNEEATG	319
IKSDLVNEEATGQ	320
VIKSDLVNEEAT	321
IKSDLVNEEATG	322
KSDLVNEEATGQ	323
VIKSDLVNEEA	344
IKSDLVNEEAT	325
KSDLVNEEATG	326
SDLVNEEATGQ	327
VIKSDLVNEE	328
IKSDLVNEEA	329
KSDLVNEEAT	330
SDLVNEEATG	331
DLVNEEATGQ	332
VIKSDLVNE	333
IKSDLVNEE	334
KSDLVNEEA	335
SDLVNEEAT	336
DLVNEEATG	337
LVNEEATGQ	338
VIKSDLVN	339
IKSDLVNE	340
KSDLVNEE	341
SDLVNEEA	342
DLVNEEAT	343
LVNEEATG	344
VNEEATGQ	345
VIKSDLV	346
IKSDLVN	347
KSDLVNE	348
SDLVNEE	349
DLVNEEA	350
LVNEEAT	351

VNEEATG	352
NEEATGQ	353
VIKSDL	354
IKSDLV	355
KSDLVN	356
SDLVNE	357
DLVNEE	358
LVNEEA	359
VNEEAT	360
NEEATG	361
EEATGQ	362
VIKSD	363
IKSDL	364
KSDLV	365
SDLVN	366
DLVNE	367
LVNEE	368
VNEEA	369
NEEAT	370
EEATG	371
EATGQ	372
VIKS	373
IKSD	374
KSDL	375
SDLV	376
DLVN	377
LVNE	378
VNEE	379
NEEA	380
EEAT	381
EATG	382
ATGQ	383
VIK	
IKS	
KSD	
SDL	
DLV	
LVN	
VNE	
NEE	
EEA	

EAT	
ATG	
TGQ	
VI	
IK	
KS	
SD	
DL	
LV	
VN	
NE	
EE	
EA	
AT	
TG	
GQ	

Table X: Short parts of Peptide CD66a-15 = SDPVTLNVTYGPDT

Amino Acid Sequence	SEQ ID NO:
SDPVTLNVTYGPDT	116
SDPVTLNVTYGPD	384
DPVTLNVTYGPDT	385
SDPVTLNVTYGP	386
DPVTLNVTYGPD	387
PVTLNVTYGPDT	388
SDPVTLNVTYG	389
DPVTLNVTYGP	390
PVTLNVTYGPD	391
VTLNVTYGPDT	392
SDPVTLNVTY	393
DPVTLNVTYG	394
PVTLNVTYGP	395
VTLNVTYGPD	396
TLNVTYGPDT	397
SDPVTLNVT	398
DPVTLNVTY	399
PVTLNVTYG	400
VTLNVTYGP	401
TLNVTYGPD	402
LNVTYGPDT	403
SDPVTLNV	404
DPVTLNVT	405
PVTLNVTY	406
VTLNVTYG	407
TLNVTYGP	408
LNVTYGPD	409
NVTYGPDT	410
SDPVTLN	411
DPVTLNV	412
PVTLNVT	413
VTLNVTY	414
TLNVTYG	415
LNVTYGP	416

NVTYGPD	417
VTYGPDT	418
SDPVTL	419
DPVTLN	420
PVTLNV	421
VTLNVT	422
TLNVTY	423
LNVTYG	424
NVTYGP	425
VTYGPD	426
TYGPDT	427
SDPVT	428
DPVTL	429
PVTLN	430
VTLNV	431
TLNVT	432
LNVTY	433
NVTYG	434
VTYGP	435
TYGPD	436
YGPDT	437
SDPV	438
DPVT	439
PVTL	440
VTLN	441
TLNV	442
LNVT	443
NVTY	444
VTYG	445
TYGP	446
YGPD	447
GPDT	448
SDPV	449
DPVT	450
PVTL	451
VTLN	452
TLNV	453
LNVT	454
NVTY	455
VTYG	456
TYGP	457

YGPD	458
GPDT	459
SDPV	
DPV	
PVT	
VTL	
TLN	
LNV	
NVT	
VTY	
TYG	
YGP	
GPD	
PDT	
DP	
PV	
VT	
TL	
LN	
NV	
VT	
TY	
YG	
GP	
PD	
DT	

Table XI: Short parts of Peptide CD66a-19 = CD66e-21 = FIPNITVNNSGSYT

Amino Acid Sequence	SEQ ID NO:
FIPNITVNNSGSYT	120
FIPNITVNNSGSY	460
IPNITVNNSGSYT	461
FIPNITVNNSGS	462
IPNITVNNSGSY	463
PNITVNNSGSYT	464
FIPNITVNNSG	465
IPNITVNNSGS	466
PNITVNNSGSY	467
NITVNNSGSYT	468
FIPNITVNNS	469
IPNITVNNSG	470
PNITVNNSGS	471
NITVNNSGSY	472
ITVNNSGSYT	473
FIPNITVNN	474
IPNITVNNS	475
PNITVNNSG	476
NITVNNSGS	477
ITVNNSGSY	478
TVNNSGSYT	479
FIPNITVN	480
IPNITVNN	481
PNITVNNS	482
NITVNNSG	483
ITVNNSGS	484
TVNNSGSY	485
VNNSGSYT	486
FIPNITV	487
IPNITVN	488
PNITVNN	489
NITVNNS	490
ITVNNSG	491

TVNNSGS	492
VNNSGSY	493
NNSGSYT	494
FIPNIT	495
IPNITV	496
PNITVN	497
NITVNN	498
ITVNNS	499
TVNNSG	500
VNNSGS	501
NNSGSY	502
NSGSYT	503
FIPNI	504
IPNIT	505
PNITV	506
NITVN	507
ITVNN	508
TVNNS	509
VNNSG	510
NNSGS	511
NSGSY	512
SGSYT	513
FIPN	514
IPNI	515
PNIT	516
NITV	517
ITVN	518
TVNN	519
VNNS	520
NNSG	521
NSGS	522
SGSY	523
GSYT	524
FIP	
IPN	
PNI	
NIT	
ITV	
TVN	
VNN	
NNS	

NSG	
SGS	
GSY	
SYT	
FI	
IP	
PN	
NI	
IT	
TV	
VN	
NN	
NS	
SG	
GS	
SY	
YT	

Table XII: Short parts of Peptide CD66a-6L = CD66c-6L = TIYPNASLLIQNVT

Amino Acid Sequence	SEQ ID NO:
TIYPNASLLIQNVT	124
TIYPNASLLIQNV	525
IYPNASLLIQNVT	526
TIYPNASLLIQN	527
IYPNASLLIQNV	528
YPNASLLIQNVT	529
TIYPNASLLIQ	530
IYPNASLLIQN	531
YPNASLLIQNV	532
PNASLLIQNVT	533
TIYPNASLLI	534
IYPNASLLIQ	535
YPNASLLIQN	536
PNASLLIQNV	537
NASLLIQNVT	538
TIYPNASLL	539
IYPNASLLI	540
YPNASLLIQ	541
PNASLLIQN	542
NASLLIQNV	543
ASLLIQNVT	544
TIYPNASL	545
IYPNASLL	546
YPNASLLI	547
PNASLLIQ	548
NASLLIQN	549
ASLLIQNV	550
SLLIQNVT	551
TIYPNAS	552
IYPNASL	553
YPNASLL	554
PNASLLI	555
NASLLIQ	556

ASLLIQN	557
SLLIQNV	558
LLIQNVT	559
TIYPNA	560
IYPNAS	561
YPNASL	562
PNASLL	563
NASLLI	564
ASLLIQ	565
SLLIQN	566
LLIQNV	567
LIQNVT	568
TIYPN	569
IYPNA	570
YPNAS	571
PNASL	572
NASLL	573
ASLLI	574
SLLIQ	575
LLIQN	576
LIQNV	577
IQNVT	578
TIYP	579
IYPN	580
YPNA	581
PNAS	582
NASL	583
ASLL	584
SLLI	585
LLIQ	586
LIQN	587
IQNV	588
QNVT	589
TIY	
IYP	
YPN	
PNA	
NAS	
ASL	
SLL	
LLI	

LIQ	
IQN	
QNV	
NVT	
TI	
IY	
YP	
PN	
NA	
AS	
SL	
LL	
LI	
IQ	
QN	
NV	
VT	

Table XIII: Short parts of Peptide CD66e-2 = CD66d-2 = LVHNLPQHLFGYSW

Amino Acid Sequence	SEQ ID NO:
LVHNLPQHLFGYSW	140
LVHNLPQHLFGYS	590
VHNLPQHLFGYSW	591
LVHNLPQHLFGY	592
VHNLPQHLFGYS	593
HNLPQHLFGYSW	594
LVHNLPQHLFG	595
VHNLPQHLFGY	596
HNLPQHLFGYS	597
NLPQHLFGYSW	598
LVHNLPQHLF	599
VHNLPQHLFG	600
HNLPQHLFGY	601
NLPQHLFGYS	602
LPQHLFGYSW	603
LVHNLPQHL	604
VHNLPQHLF	605
HNLPQHLFG	606
NLPQHLFGY	607
LPQHLFGYS	608
PQHLFGYSW	609
LVHNLPQH	610
VHNLPQHL	611
HNLPQHLF	612
NLPQHLFG	613
LPQHLFGY	614
PQHLFGYS	615
QHLFGYSW	616
LVHNLPQ	216
VHNLPQH	617
HNLPQHL	618
NLPQHLF	619
LPQHLFG	620

PQHLFGY	621
QHLFGYS	622
HLFGYSW	623
LVHNLP	224
VHNLPQ	225
HNLPQH	624
NLPQHL	625
LPQHLF	626
PQHLFG	627
QHLFGY	628
HLFGYS	629
LFGYSW	232
LVHNL	233
VHNLP	234
HNLPQ	235
NLPQH	630
LPQHL	631
PQHLF	632
QHLFG	633
HLFGY	634
LFGYS	241
FGYSW	242
LVHN	243
VHNL	244
HNLP	245
NLPQ	246
LPQH	635
PQHL	636
QHLF	637
HLFG	638
LFGY	251
FGYS	252
GYSW	253
LVH	
VHN	
HNL	
NLP	
LPQ	
PQH	
QHL	
HLF	

LFG	
FGY	
GYS	
YSW	
LV	
VH	
HN	
NL	
LP	
PQ	
QH	
HL	
LF	
FG	
GY	
YS	
SW	

Table XIV: Short parts of Peptide CD66e-3 = KGERVDGNRQIIGY

Amino Acid Sequence	SEQ ID NO:
KGERVDGNRQIIGY	131
KGERVDGNRQIIG	639
GERVDGNRQIIGY	640
KGERVDGNRQII	641
GERVDGNRQIIG	642
ERVDGNRQIIGY	643
KGERVDGNRQI	259
GERVDGNRQII	644
ERVDGNRQIIG	645
RVDGNRQIIGY	646
KGERVDGNRQ	263
GERVDGNRQI	264
ERVDGNRQII	647
RVDGNRQIIG	648
VDGNRQIIGY	649
KGERVDGNR	268
GERVDGNRQ	269
ERVDGNRQI	270
RVDGNRQII	650
VDGNRQIIG	651
DGNRQIIGY	652
KGERVDGN	274
GERVDGNR	275
ERVDGNRQ	276
RVDGNRQI	277
VDGNRQII	653
DGNRQIIG	654
GNRQIIGY	655
KGERVDG	281
GERVDGN	282
ERVDGNR	283
RVDGNRQ	284
VDGNRQI	285
DGNRQII	656

GNRQIIG	657
NRQIIGY	658
KGERVD	289
GERVDG	290
ERVDGN	291
RVDGNR	292
VDGNRQ	293
DGNRQI	294
GNRQII	659
NRQIIG	660
RQIIGY	661
KGERV	298
GERVD	299
ERVDG	300
RVDGN	301
VDGNR	302
DGNRQ	303
GNRQI	304
NRQII	662
RQIIG	663
QIIGY	664
KGER	308
GERV	309
ERVD	310
RVDG	311
VDGN	312
DGNR	313
GNRQ	314
NRQI	315
RQII	665
QIIG	666
IIGY	667
KGE	
GER	
ERV	
RVD	
VDG	
DGN	
GNR	
NRQ	
RQI	

QII	
IIG	
IGY	
KG	
GE	
ER	
RV	
VD	
DG	
GN	
NR	
RQ	
QI	
II	
IG	

Table XV: Short parts of Peptide CD66e-19 = AASNPPAQYSWFVN

Amino Acid Sequence	SEQ ID NO:
AASNPPAQYSWFVN	132
AASNPPAQYSWFV	668
ASNPPAQYSWFVN	669
AASNPPAQYSWF	670
ASNPPAQYSWFV	671
SNPPAQYSWFVN	672
AASNPPAQYSW	673
ASNPPAQYSWF	674
SNPPAQYSWFV	675
NPPAQYSWFVN	676
AASNPPAQYS	677
ASNPPAQYSW	678
SNPPAQYSWF	679
NPPAQYSWFV	680
PPAQYSWFVN	681
AASNPPAQY	682
ASNPPAQYS	683
SNPPAQYSW	684
NPPAQYSWF	685
PPAQYSWFV	686
PAQYSWFVN	687
AASNPPAQ	688
ASNPPAQY	689
SNPPAQYS	690
NPPAQYSW	691
PPAQYSWF	692
PAQYSWFV	693
AQYSWFVN	694
AASNPPA	695
ASNPPAQ	696
SNPPAQY	697
NPPAQYS	698
PPAQYSW	699
PAQYSWF	700

AQYSWFV	701
QYSWFVN	702
AASNPP	703
ASNPPA	704
SNPPAQ	705
NPPAQY	706
PPAQYS	707
PAQYSW	708
AQYSWF	709
QYSWFV	710
YSWFVN	711
AASNP	712
ASNPP	713
SNPPA	714
NPPAQ	715
PPAQY	716
PAQYS	717
AQYSW	718
QYSWF	719
YSWFV	720
SWFVN	721
AASN	722
ASNP	723
SNPP	724
NPPA	725
PPAQ	726
PAQY	727
AQYS	728
QYSW	729
YSWF	730
SWFV	731
WFVN	732
AAS	
ASN	
SNP	
NPP	
PPA	
PAQ	
AQY	
QYS	
YSW	

SWF	
WFV	
FVN	
AA	
AS	
SN	
NP	
PP	
PA	
AQ	
QY	
YS	
SW	
WF	
FV	
VN	

Table XVI: Short parts of Peptide CD66e-31 = SVDHSDPVILNVLY

Amino Acid Sequence	SEQ ID NO:
SVDHSDPVILNVLY	133
SVDHSDPVILNVL	733
VDHSDPVILNVLY	734
SVDHSDPVILNV	735
VDHSDPVILNVL	736
DHSDPVILNVLY	737
SVDHSDPVILN	738
VDHSDPVILNV	739
DHSDPVILNVL	740
HSDPVILNVLY	741
SVDHSDPVIL	742
VDHSDPVILN	743
DHSDPVILNV	744
HSDPVILNVL	745
SDPVILNVLY	746
SVDHSDPVI	747
VDHSDPVIL	748

DHSDPVILN	749
HSDPVILNV	750
SDPVILNVL	751
DPVILNVLY	752
SVDHSDPV	753
VDHSDPVI	754
DHSDPVIL	755
HSDPVILN	756
SDPVILNV	757
DPVILNVL	758
PVILNVLY	759
SVDHSDP	760
VDHSDPV	761
DHSDPVI	762
HSDPVIL	763
SDPVILN	764
DPVILNV	765
PVILNVL	766
VILNVLY	767
SVDHSD	768
VDHSDP	769
DHSDPV	770
HSDPVI	771
SDPVIL	772
DPVILN	773
PVILNV	774
VILNVL	775
ILNVLY	776
SVDHS	777
VDHSD	778
DHSDP	779
HSDPV	780
SDPVI	781
DPVIL	782
PVILN	783
VILNV	784
ILNVL	785
LNVLY	786
SVDH	787
VDHS	788

DHSD	789
HSDP	790
SDPV	438
DPVI	791
PVIL	792
VILN	793
ILNV	794
LNVL	795
NVLY	796
SVD	
VDH	
DHS	
HSD	
SDP	
DPV	
PVI	
VIL	
ILN	
LNV	
NVL	
VLY	
SV	
VD	
DH	
HS	
SD	
DP	
PV	
VI	
IL	
LN	
NV	
VL	
LY	

Table XVII: Short parts of Peptide CD66e-42 = PEAQNTTYLWWVNG

Amino Acid Sequence	SEQ ID NO:
PEAQNTTYLWWVNG	134
PEAQNTTYLWWVN	797
EAQNTTYLWWVNG	798
PEAQNTTYLWWV	799
EAQNTTYLWWVN	800
AQNTTYLWWVNG	801
PEAQNTTYLWW	802
EAQNTTYLWWV	803
AQNTTYLWWVN	804
QNTTYLWWVNG	805
PEAQNTTYLW	806
EAQNTTYLWW	807
AQNTTYLWWV	808
QNTTYLWWVN	809
NTTYLWWVNG	810
PEAQNTTYL	811
EAQNTTYLW	812
AQNTTYLWW	813
QNTTYLWWV	814
NTTYLWWVN	815
TTYLWWVNG	816
PEAQNTTY	817
EAQNTTYL	818
AQNTTYLW	819
QNTTYLWW	820
NTTYLWWV	821
TTYLWWVN	822
TYLWWVNG	823
PEAQNTT	824
EAQNTTY	825
AQNTTYL	826
QNTTYLW	827
NTTYLWW	828
TTYLWWV	829

TYLWWVN	830
YLWWVNG	831
PEAQNT	832
EAQNTT	833
AQNTTY	834
QNTTYL	835
NTTYLW	836
TTYLWW	837
TYLWWV	838
YLWWVN	839
LWWVNG	840
PEAQN	841
EAQNT	842
AQNTT	843
QNTTY	844
NTTYL	845
TTYLW	846
TYLWW	847
YLWWV	848
LWWVN	849
WWVNG	850
PEAQ	851
EAQN	852
AQNT	853
QNTT	854
NTTY	855
TTYL	856
TYLW	857
YLWW	858
LWWV	859
WWVN	860
WVNG	861
PEA	
EAQ	
AQN	
QNT	
NTT	
TTY	
TYL	
YLW	
LWW	

WWV	
WVN	
VNG	
PE	
EA	
AQ	
QN	
NT	
TT	
TY	
YL	
LW	
WW	
WV	
VN	
NG	

BRIEF DESCRIPTION OF DRAWINGS

Figure 1. Effects of CD66a peptides on T-cell activation by anti-CD3. T-cells were added to media containing the indicated CD66a peptide S28 ((CD66a-24), (SEQ ID NO:1)) at 150 μg/ml (final concentration) or positive or negative controls in 96 well microtiter plates, and the plates were incubated at 37°C for 30 min in 5% CO_2. Media containing anti-CD3 anitbody was then added and the cells were incubated at 37° for 30 min in 5% CO_2 for 56 hours. Twenty μl of media containing 1 μCi of ^{3}H-Tdr was then added to each well and the plates were incubated at 37°C for 30 min in 5% CO_2 for an additional 16 hours. The cells were then harvested onto glass fiber filter papers and the radioactivity incorporated into the cells was then determined by liquid scintillation counting. Values are shown as the amount of ^{3}H-Tdr incorporation in the presence of the indicated peptide as a percent of that incorpoated in the absence of peptide, and represent the means +/- SD of 4 separate determinations. The T-cell

proliferation observed in the presence of the active CD66a peptide S28 was statistically less than that observed with media alone (positive control) ($p<0.05$).

Figure 2. Effects of scrambled S28 peptides on T-cell activation by anti-CD3. T-cells were stimulated with anti-CD3 antibody, and proliferation was quantitated by ^{3}H-Tdr incorporation in the presence of the two scrambled versions of the S28 peptide (S159 and S160) at 150 μg/ml (final concentration) as described in Figure 1. Values are shown as the amount of ^{3}H-Tdr incorporation in the presence of the indicated concentration of peptide as a percent of that incorpoated in the absence of peptide, and represent the means +/- SD of 4 separate determinations. The cell proliferation observed in the presence of the active S28 peptide shown in Fig 1, was statistically less than that observed with the 2 scrambled peptides shown here ($p<0.05$). [S159 = GIWRFSKDFTINTN (SEQ ID NO:2); S160 = KIDNFTSNGFTIWR (SEQ ID NO:3)].

Figure 3. Effects of smaller fragments of the S28 peptide on T-cell activation by anti-CD3. To further analyze the activity of the S28 peptide, three smaller fragments of the active peptide were made and tested in the T-cell activation assay as in Fig 1. Each of the smaller peptides (S180, S181, and S182) had activity in the T-cell activation assay (Fig. 3), demonstrating that the entire amino acid sequence of S28 is not required for activity. [S180 = TNDTGIS (SEQ ID NO:4); S181 = TGISIRW (SEQ ID NO:5); S182 = IRWFFKN (SEQ ID NO:6)].

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

Because of the adhesive and signaling properties of CD66 (CEACAM) family members described above, we sought to identify functionally active domains of CD66 (CEACAM) family members by use of synthetic peptides. In earlier work (PCT/US00/23482), peptides of 14 amino acids in length were

synthesized and investigated for the ability to modulate the function of CD66 (CEACAM) family members. The present invention provides isolated peptides that include the amino acid sequence shown in the attached tables, or analogs thereof, that modulate the function of at least one CD66 protein (i.e., CD66 family member) and/or at least one ligand thereof. The active peptides could mediate direct binding of natural CD66 family members.

Peptides were also tested for their ability to inhibit the activation of T-cells toward proliferation and/or differentiation. One peptide, hereafter termed peptide S28 (SEQ ID NO:1), was found to be a potent inhibitor of T-cell activation, and smaller fragments of this peptide also had similar activity. Modulating the immune response, as for example by activating or inhibiting the proliferation and/or differentiation of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells, may be useful in treating autoimmune diseases, and in transplantation therapies where graft vs. host or host vs. graft effects may be undesirable. The peptides could also be immune stimulants in settings such as cancer, infectious disease, or immunization. Alternatively, they could be immune suppressants. They could also be used to detect inflammation, and preferably modulate inflammation by activating or inhibiting activation of immune or inflammatory cells. A preferred method involves detecting (and preferably modulating) inflammation in tissues such as inflamed vasculature or leukocytes.

Thus, preferably, the present invention provides isolated peptides shown in the attached tables. It is also believed that these would have activity if they were solubilized or conjugated in a complex.

Thus, the present invention provides peptides derived from CD66 (CEACAM) family members that are capable of modulating (i.e., altering by increasing, decreasing, etc.), for example, cell activation, cell adhesion, cell proliferation, cell differentiation, or homotypic and/or heterotypic adhesion among CD66 family members or binding of CD66 family members to their ligands.

In addition to the peptides discussed above that are specifically shown to have such activity, others are believed to possess a least one activity as described herein. These peptides are shown in the attached tables.

Compositions comprising the polypeptides of this invention can be added to cells in culture (*in vitro*) or used to treat patients, such as mammals (*in vivo*). Where the polypeptides are used to treat a patient, the polypeptide is preferably combined in a pharmaceutical composition with a pharmaceutically acceptible carrier such as a larger molecule to promote polypeptide stability or a pharmaceutically acceptible buffer that serves as a carrier for the polypeptide or incorporated in a peptide conjugate that has more than one peptide coupled to a single entity.

Given the known bacterial and viral binding properties of CD66 family members, the peptides described herein could be useful for altering the binding of viruses, bacteria, or other pathological etiologic agents to the cells of host tissues, transplanted tissues, or to biomaterials (increase or inhibit binding). They could also be useful for detecting a CD66 protein or a ligand thereof in tissue, whether it be *in vitro* or *in vivo*.

Studies were also performed to demonstrate that these peptides could be used to target the binding of larger structures to cells expressing the appropriate CD66 family member. The coupling of multiple copies of peptides to larger structures (thereby forming peptide conjugates) allows cooperativity of binding due to the presence of multiple binding sites. This markedly increases the affinity of binding of the complex compared with that of a single free peptide. In addition, it should therefore be possible to complex various combinations and densities of different peptides described herein to create a structure that preferentially binds cells expressing a specific pattern of CD66 family members.

The biological activity of the peptides identified here suggests that they have sufficient affinity to make them potential candidates for drug localization to cells expressing the appropriate surface structures. This targeting and binding to cells could be useful for the delivery of therapeutically active agents (including targeting drugs, DNA sequences, RNA sequences, lipids, proteins

(e.g., human growth factors)) and gene therapy/gene delivery. More preferably, the therapeutically active agent is an antibacterial agent, antiinflammatory agent, or antineoplastic agent.

Since different cells, including specifically many malignant cells, cells of different tissues, growing endothelial cells, including endothelial cells in new vessels in tumors and in diabetic proliferative microvasculature, express different combinations of CD66 family members, it should be possible to generate compounds bearing different combinations of densities of CD66 peptides that would target (bind preferentially) to different desired tissues or cells.

As proof of principle, the peptide S28 when coupled to microbeads directs the binding of the complexed microbeads to CHO cells expressing CD66a.

Also, CD66 family members have been shown to alter metastases of malignant cells and can alter cell differentiation. Thus, the peptides described herein could modify the process of metastasis of malignant cells either by altering the behavior of the malignant cells directly, or by altering the physiology of a target tissue (as for example, the liver where CD66e has been shown to alter cytokine production by cells in the liver and also alter the ability of colon cancer cells to metastasize to the liver). The peptides described herein can also be used in detecting tumors.

Thus, the peptides described herein are believed to be useful for altering angiogenesis. In such a method, endothelial cells, tumor cells, or immune cells are contacted with at least one peptide described herein.

Some CD66 members are expressed in growing keratinocytes at the edge of healing wounds. These peptides may be useful to alter keratinocyte growth or behavior or the behavior of other cell involved in wound healing.

These peptides may be useful in altering the growth or physiology of cells, which are in various disease states, that can express CD66 members, including gut (as for example in inflammatory bowel disease, atrophic states, or cancer), breast, stomach, small bowel, colon, pancreas, thyroid, prostate, lung, kidney, placenta, sebaceous glands, and uterus.

Treatment for these various conditions can be prophylactic or therapeutic. Thus, treatment can be initiated before, during, or after the development of the condition. As such, the phrases "inhibition of" or "effective to inhibit" a condition includes both prophylactic and therapeutic treatment (i.e., prevention and/or reversal of the condition).

Additionally, molecules/particles with a specific number of specific CD66 peptides would bind specifically to cells/tissues expressing specific ligand combinations, and therefore could have diagnostic and therapeutic use. Thus, the peptides of the present invention can be labeled (e.g., fluorescent, radioactive, enzyme, nuclear magnetic) and used to detect specific targets *in vivo* or *in vitro* including "immunochemistry" like assays *in vitro*. *In vivo* they could be used in a manner similar to nuclear medicine imaging techniques to detect tissues, cells, or other material expressing specific CD66 ligands.

The polypeptides shown in the attached tables can be in their free acid form or they can be amidated at the C-terminal carboxylate group. The present invention also includes analogs of the polypeptides shown in the attached tables, which typically have structural similarity with the sequences shown in the attached tables. An "analog" of a polypeptide includes at least a portion of the polypeptide, wherein the portion contains deletions or additions of one or more contiguous or noncontiguous amino acids, or containing one or more amino acid substitutions. Substitutes for an amino acid in the polypeptides of the invention are preferably conservative substitutions, which are selected from other members of the class to which the amino acid belongs. An analog can also be a larger peptide that incorporates the peptides described herein. For example, it is well-known in the art of protein biochemistry that an amino acid belonging to a grouping of amino acids having a particular size or characteristic (such as charge, hydrophobicity and hydrophilicity) can generally be substituted for another amino acid without substantially altering the structure of a polypeptide.

For the purposes of this invention, conservative amino acid substitutions are defined to result from exchange of amino acids residues from within one of the following classes of residues: Class I: Ala, Gly, Ser, Thr, and Pro; Class II: Cys, Ser, Thr, and Tyr; Class III: Glu, Asp, Asn, and Gln (carboxyl group

containing side chains): Class IV: His, Arg, and Lys (representing basic side chains); Class V: Ile, Val, Leu, Phe, and Met (representing hydrophobic side chains); and Class VI: Phe, Trp, Tyr, and His (representing aromatic side chains). The classes also include other related amino acids such as halogenated tyrosines in Class VI.

Polypeptide analogs, as that term is used herein, also include modified polypeptides. Modifications of polypeptides of the invention include chemical and/or enzymatic derivatizations at one or more constituent amino acid, including side chain modifications, backbone modifications, and N- and C-terminal modifications including acetylation, hydroxylation, methylation, amidation, and the attachment of carbohydrate or lipid moieties, cofactors, and the like.

A preferred polypeptide analog is characterized by having at least one of the biological activities described herein. Such an analog is referred to herein as a "biologically active analog" or simply "active analog." The biological activity of a polypeptide can be determined, for example, as described in the Examples Section.

The polypeptides of the invention may be synthesized by the solid phase method using standard methods based on either t-butyloxycarbonyl (BOC) or 9-fluorenylmethoxy-carbonyl (FMOC) protecting groups. This methodology is described by G.B. Fields et al. in Synthetic Peptides: A User's Guide, W.M. Freeman & Company, New York, NY, pp. 77-183 (1992). The present peptides may also be synthesized via recombinant techniques well known to those skilled in the art. For example, U.S. Patent No. 5,595,887 describes methods of forming a variety of relatively small peptides through expression of a recombinant gene construct coding for a fusion protein which includes a binding protein and one or more copies of the desired target peptide. After expression, the fusion protein is isolated and cleaved using chemical and/or enzymatic methods to produce the desired target peptide.

The peptides of the present invention may be employed in a monovalent state (e.g., free peptide or peptide coupled to a carrier molecule or structure). The peptides may also be employed as conjugates having more than one (same

or different) peptide bound to a single carrier molecule. The carrier molecule or structure may be microbeads, liposomes, biological carrier molecule (e.g., a glycosaminoglycan, a proteoglycan, albumin, or the like), a synthetic polymer (e.g., a polyalkyleneglycol or a synthetic chromatography support), biomaterial (e.g., a material suitable for implantation into a mammal or for contact with biological fluids as in an extrcorporeal device), or other cell. Typically, ovalbumin, human serum albumin, other proteins, polyethylene glycol, or the like are employed as the carrier. Such modifications may increase the apparent affinity and/or change the stability of a peptide. The number of peptide fragments associated with or bound to each carrier can vary. In addition, as mentioned above, the use of various mixtures and densities of the peptides described herein may allow the production of complexes that have specific binding patterns in terms of preferred ligands.

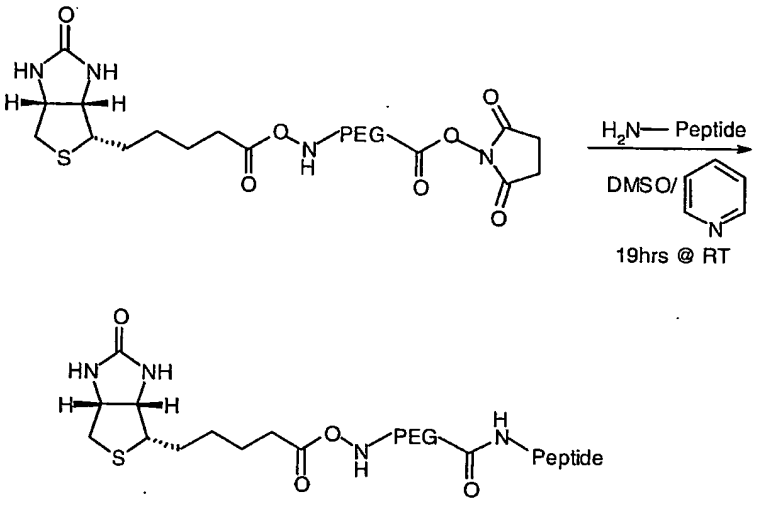
The polypeptides can be conjugated to other polypeptides using standard methods known to one of skill in the art. Conjugates can be separated from free peptide through the use of gel filtration column chromatography or other methods known in the art.

For instance, peptide conjugates may be prepared by treating a mixture of peptides and carrier molecules (or structures) with a coupling agent, such as a carbodiimide. The coupling agent may activate a carboxyl group on either the peptide or the carrier molecule (or structure) so that the carboxyl group can react with a nucleophile (e.g. an amino or hydroxyl group) on the other member of the peptide conjugate, resulting in the covalent linkage of the peptide and the carrier molecule (or structure).

As another example, peptides may be coupled to biotin-labeled polyethylene glycol and then coupled to avidin containing compounds, for instance. Peptides are weighed out in aliquots of 0.5 mg and dissolved in a total volume of 500 µl dimethyl sulfoxide (DMSO, FisherChemical, Fair Lawn, NJ) in a 1 mL ReactiVial containing a stir bar. To each ReactiVial, 1.0 mg Biotin-PEG-NHS, average MW 3400, (Shearwater Polymers, Huntsville, AL) is added directly and the vial is moved to a stir plate to provide gentle mixing. Pyridine (Sigma Chemical, St. Louis, MO) is added as a basic catalyst at a 5% molar

excess to the peptide. The reaction is allowed to proceed for 19 hours at room temperature with medium stirring.

After completion of the reaction, the contents of each ReactiVial are individually transferred to a 1.5 mL plastic microfuge tube. Each vial is washed once with 25 µl DMSO which is also added to the microfuge tube. The volume of DMSO is dried down at room temperature to approximately 20 µl of remaining solvent in a Savant Speed Vac Plus. To each tube individually, 980 µl of Hanks balanced salt solution (HBSS) + 0.1% sodium azide is added. Samples are stored at –20°C until coupling to streptavidin-coated beads.



Reaction scheme for boitinylation of peptides.

Streptavidin-coated 6 µm diameter polystyrene beads are obtained from Polysciences (Warrington, PA). For each peptide, 100 µl of suspended beads are aliquoted to a 1.5 ml plastic microfuge tube. As per the manufacturer's directions, the beads are washed three times by sequentially pelleting the beads in a microcentrifuge, decanting the supernatant and redispersing them in 1 ml of fresh phosphate buffered saline (PBS). One third (333 µl) of the biotinylated peptide from the above preparation is added to the beads in a total volume of 1 ml. From the reported binding capacity of the streptavidin-coated beads, this amount of pegylated peptide respresents more than a two-fold molar excess,

thus the biotin binding sites are believed to be saturated. The tubes are mixed end-to-end on a rocker plate at 100 revolutions per minute (RPM) for 1 hour. The beads are then washed once as before and resuspended in 1 ml of a 0.1 M ethanolamine solution and mixed on the rocker plate as before for 30 minutes. This step serves to block any potentially unreacted NHS moieties. The beads are again washed once as before and resuspended in HBSS + 0.1% sodium azide. In the case of peptides coupled to other entities, it should be understood that the designed activity may depend on which end of the peptide is coupled to the entity.

The present invention also provides a composition that includes one or more active agents (i.e., polypeptides) of the invention and one or more pharmaceutically acceptable carriers. One or more polypeptides with demonstrated biological activity can be administered to a patient in an amount alone or together with other active agents and with a pharmaceutically acceptable buffer. The polypeptides can be combined with a variety of physiological acceptable carriers for delivery to a patient including a variety of diluents or excipients known to those of ordinary skill in the art. For example, for parenteral administration, isotonic saline is preferred. For topical administration, a cream, including a carrier such as dimethylsulfoxide (DMSO), or other agents typically found in topical creams that do not block or inhibit activity of the peptide, can be used. Other suitable carriers include, but are not limited to alcohol, phosphate buffered saline, and other balanced salt solutions.

The formulations may be conveniently presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. Preferably, such methods include the step of bringing the active agent into association with a carrier that constitutes one or more accessory ingredients.

The methods of the invention include administering to a patient, preferably a mammal, and more preferably a human, the composition of the invention in an amount effective to produce the desired effect.

The peptides can be administered as a single dose or in multiple doses. Useful dosages of the active agents can be determined by comparing their *in vitro* activity and the *in vivo* activity in animal models. Methods for

extrapolation of effective dosages in mice, and other animals, to humans are known in the art.

The agents of the present invention are preferably formulated in pharmaceutical compositions and then, in accordance with the methods of the invention, administered to a patient, such as a human patient, in a variety of forms adapted to the chosen route of administration. The formulations include, but are not limited to, those suitable for oral, rectal, vaginal, topical, nasal, ophthalmic, or parental (including subcutaneous, intramuscular, intraperitoneal, intratumoral, intraorgan, intraarterial and intravenous) administration.

Formulations suitable for parenteral administration conveniently include a sterile aqueous preparation of the active agent, or dispersions of sterile powders of the active agent, which are preferably isotonic with the blood of the recipient. Absorption of the active agents over a prolonged period can be achieved by including agents for delaying, for example, aluminum monostearate and gelatin.

Formulations of the present invention suitable for oral administration may be presented as discrete units such as tablets, troches, capsules, lozenges, wafers, or cachets, each containing a predetermined amount of the active agent as a powder or granules, as liposomes containing the active agent, or as a solution or suspension in an aqueous liquor or non-aqueous liquid such as a syrup, an elixir, an emulsion, or a draught. Such compositions and preparations typically contain at least about 0.1 wt-% of the active agent. The amount of polypeptide (i.e., active agent) is such that the dosage level will be effective to produce the desired result in the patient.

Nasal spray formulations include purified aqueous or other solutions of the active agent with preservative agents and isotonic agents. Such formulations are preferably adjusted to a pH and isotonic state compatible with the nasal mucous membranes. Formulations for rectal or vaginal administration may be presented as a suppository with a suitable carrier such as cocoa butter, or hydrogenated fats or hydrogenated fatty carboxylic acids. Ophthalmic formulations are prepared by a similar method to the nasal spray, except that the pH and isotonic factors are preferably adjusted to match that of the eye. Topical

formulations include the active agent dissolved or suspended in one or more media such as mineral oil, petroleum, polyhydroxy alcohols, or other bases used for topical pharmaceutical formulations.

EXAMPLES

Materials and Methods

Cell Preparation. Peripheral blood mononuclear cells (PBMC) were isolated by centrifugation of heparinized blood on a Ficoll/Hypaque (Pharmacia, Uppsala, Sweden) density gradient. Cells from the interface of the gradient were harvested, and resuspended at a concentration of 10^6/ml in medium [RPMI-1640 supplemented with 10% heat inactivated fetal bovine serum, 2 mM L-glutamine, 10 mM HEPES buffer, pH 7.4, 100 U/ml penicillin and 100 ug/ml streptomycin (Gibco, Paisley, U.K.)]. To isolate T-cells, adherent cells were eliminated from PBMC by culture for one hour at 37°C in 5% CO_2 on tissue culture-treated plastic. Remaining B-cells, monocytes, and NK cells were deleted by immunomagnetic negative selection using anti-CD14, anti-CD19, and anti-CD56 microbeads per the manufacturer's recommendations (Miltenyi Biotec GMBH, Bergisch Gladbach, Germany). The purity of the isolated T-cells was > 90% as assessed by flow cytometry using FITC-labeled anti-CD3 (Pharmingen, Hamburg, Germany).

Peptide selection, synthesis, and purification. CEACAM1 was modeled to conform to the IgV and Ig C2 domains of the heavy and light chains of Fab fragments of immunoglobulin and CD4, and appropriate peptides were identified as previously reported in the International Patent Application Serial No. PCT/US00/23482 (filed August 26, 2000).

Peptides were synthesized as amides by Fmoc solid-phase methodology on a Gilson Automated Multiple Peptide Synthesizer AMS 422. Peptides were purified by preparative reverse phase-HPLC on a Beckman System Gold equipped with a Regis Chemical ODS C18 column (10 μm particle size, 60 A pore size, 250 x 21.1 mm). The elution gradient was 12-50% B over 35 min at a flow rate of 5.0 ml/min, where A was water containing 0.1% trifluoroacetic acid, and B was acetonitrile containing 0.1% trifluoroacetic acid. Detection was at 235 nm. Peptides were analyzed for the correct amino acid composition by

fast atom bombardment mass spectrometry, and all peptides were found to have the correct composition.

T-cell activation assay. Purified T-cells (1 x 10^5/well) were plated into flat-bottomed 96 well microtiter plates (Greiner, Frickenhausen, Germany) and peptides were added at the indicated concentration. T-cells were incubated with the peptides for 30 min and then stimulated by adding 0.3 μg/ml of anti-CD3 mAb (Pharmingen). The cells were then incubated at 37 ^oC in 5 % CO_2 for 56 hours. One μCi of tritiated thymidine (^{3}H-Tdr) (Amersham Buchler, Braunschweig, Germany) in 20 μl of RPMI-1640 was then added to each well, and the cells were cultured for another 16 hours. Cells were then harvested with a cell harvester (Pharmacia LKB-Wallac) onto glass fiber filter paper in a minifold filtration unit (Wallac, Turku, Finland). Individual filters were dissolved in scintillation fluid, and ^{3}H-Tdr incorporation was measured with a liquid scintillation counter (Pharmacia).

Example 1 - Effects of CD66 peptides on T-cell activation.

Cytotoxic lymphocytes are felt to play a key role in the immune response to malignant transformation. T-cells play an important role in the immune system, and a number of cell-surface molecules have been found to regulate T-cell activation (64-67). Thus, we tested the effects of CD66 peptides on T-cell activation as determined by proliferation following stimulation by anti-CD3.

The peptides were tested for their ability to alter T-cell activation by anti-CD3 (Fig 1). When T-cells were incubated for 30 min in the presence of media containing 150 ug/ml of each peptide, then stimulated by the addition of anti-CD3 antibody, and proliferation quantitated by ^{3}H-Tdr incorporation 16 hours after the adding ^{3}H-Tdr, as described above, peptide S28 inhibited T-cell activation by anti-CD3 compared with control (Fig 1).

Example 2 – Effects of scrambled peptides on T-cell activation.

To confirm that the activity of peptide S28 was due to the primary amino acid sequence, two scrambled versions of the active peptide S28 were

synthesized (Table I) and tested in the T-cell activation assay. In contrast to the native peptide, neither of the 2 scrambled peptides had activity in the T-cell activation assay (Fig. 2). These results show that the primary amino acid sequence of peptide S28 is essential for its functional activity, and that the biological activity was not merely due to the net charge or amino acid composition of peptide S28.

Example 3 – Effects of smaller parts of peptides on T-cell activation.

To further analyze the activity of the S28 peptide, three smaller fragments of the active peptide were synthesized (Table II) and tested in the T-cell activation assay. Each of the smaller peptides had activity in the T-cell activation assay (Fig. 3), demonstrating that the entire amino acid sequence of S28 is not required for activity.

Discussion

Peptides were synthesized from regions of CD66 family members that we predict may be exposed on the surface of the molecule. Peptide S28 was found to have activity in an assay for T-cell activation. Scrambled versions of peptide S28 had no biological activity in this assay, suggesting that the specific primary amino acid sequence is critical for activity. Smaller fragments of peptide S28 also had functional biological activity.

Several other studies have proposed structural motifs of CD66a family proteins (16, 21, 68).

Although carbohydrates on CD66 family members may play important roles, the protein backbone itself appears to have important activity in this and other studies. For example, bacterial fusion proteins free of carbohydrates containing the N or A3B3 domains of CD66e can block CD66e homotypic adhesion, demonstrating that protein-protein interaction is involved in CD66e homotypic adhesion (23). Deglycosylated forms of CD66b and CD66c retain heterotypic adhesion activity (31), further demonstrating that carbohydrates are not necessary for their adhesion functions. In addition, both recombinant N-terminal domains of CD66a and CD66e expressed in *E. coli* bind Opa proteins

with the same specificities as native CD66 molecules, and deglycosylated forms of CD66e bind bacterial Opa proteins (50).

The finding that these short peptides can alter cell activation, as can CD66a mAbs (26-28, 69-71) suggests that they have significant affinity for a surface structure, possibly native CD66a. If so, whether the activity derives from binding native CD66a and transducing a signal directly, or by another mechanism will require further study. The ability of the synthetic peptides described here to alter T-cell activation could be mediated by alterations in CD66a dimerization, possibly by disrupting a preexisting association of CD66a with other CD66 members (including CD66a itself in the form of dimers or oligomers already present on the cell surface) or by stimulating dimerization. It has been suggested that CD66a (72) and CD66e (73) exist on the cell surface as dimers. Dimerization of CD66a could potentially occur via interactions between the extracellular domains of CD66a molecules or via other mechanisms. In other receptor systems (e.g. EGF-monomeric, PDGF-dimeric), it is clear that bivalency of ligand is not necessary to induce receptor dimerization (74-77). Finally, the observed functional "inhibition" could reflect either "inhibition" per se or possibly release from a baseline stimulation.

The mechanisms by which CD66 family members transmit signals (e.g. activation in neutrophils, immune suppression of T-lymphocytes, or growth regulating signals in epithelial cells and carcinomas) are unclear. CD66a is phosphorylated in neutrophils and colon cancer cells (4, 59-61), and associated protein kinase and phosphatase activity may be involved (59, 62). At least eight isoforms of CD66a derived from differential splicing have been described (3, 12, 13, 25). These isoforms contain one N-domain, either three, two, or no Ig C2-like domains, and either a short or a long cytoplasmic tail. Only those isoforms with a long cytoplasmic tail can be phosphorylated on tyrosine, and only the isoform with four Ig domains and a long cytoplasmic tail (the ony isoform detected in neutrophils) have been implicated in signaling. The cytoplasmic domain of neutrophil CD66a contains an immune tyrosine inhibitory motif (ITIM), as well as a motif similar to ITAM (immune tyrosine activating motif) (3, 59). Phosphorylation of ITAMs and ITIMs leads to

binding of protein tyrosine kinases and protein tyrosine phosphatases, respectively, which leads to modification of signal transduction (62, 63). Calmodulin has also been found to bind to the cytoplasmic domain of CD66a, causing an inhibition of homotypic self-association of CD66a in a dot-blot assay (78). CD66a has also recently been shown to dimerize in solution, and calcium-activated calmodulin caused dissociation of CD66a dimers in vitro; suggesting that CD66a dimerization is regulated by calmodulin and intracellular calcium (72). It has been suggested that CD66a dimerization could also be influenced by phosphorylation; CD66a is phosphorylated on Thr-453 in the calmodulin binding site by protein kinase C (3). Clearly, dimerization of CD66a could affect binding of other signal regulating molecules.

CD66 family members appear to be involved in a wide variety of important biological processes, and their differential expression provides the possibility for diverse interactions. For example, CD66a, CD66b, CD66c, and CD66d, but not CD66e, are expressed on neutrophils; CD66e is expressed on many tumor cells but not leukocytes; CD66b is expressed on neutrophils but not epithelial cells; CD66c is expressed on both neutrophils and epithelial cells (reviewed in (1) and (13)). While CD66a was originally described in biliary canaliculi, it has since been found in carcinomas as well as normal tissues, including: sebaceous glands (79, 80), neutrophils, placenta, stomach, breast, pancreas, thyroid, prostate, lung, kidney, uterus, and colon (reviewed in (1) and (25)). The surface expression of these molecules in other cells may also be regulated; for example, CD66a expression is induced on HUVECs following treatment with gamma-IFN (10). In addition, surface expression of CD66 family members may be regulated by other stimuli and this may modify the signal transduction capabilities of cell surface CD66 molecules. Finally, studies have shown that certain bacteria bind to some CD66 family members on neutrophils (45-50, 81, 82) and this interaction may also result in signal transduction resulting in modification of neutrophil activity. The major receptor for murine hepatitis virus is a murine CD66a equivalent (51-55) and studies suggest that this virus uses different murine CD66 family members as the major receptor in different tissues (55). A recent consensus was reached that will

rename the CD66 antigens as follows: CD66a antigen, CEACAM-1; CD66b antigen, CEACAM-8; CD66c antigen, CEACAM-6; CD66d antigen, CEACAM-3, CD66e antigen, CEA (14).

CD66 members appear to play an important role in inflammation. Each of the CD66 family members expressed on neutrophils, CD66a, CD66b, CD66c, and CD66d, are capable of transmitting activation signals in neutrophils, and neutrophil CD66a and CD66c appear to be able to present CD15s (a ligand for ELAM-1 or E-selectin) to E-selectin on endothelial cells in a functional way (26). Recent studies have demonstrated the presence of CD66a on T-lymphocytes and a subset of NK cells (CD16-, CD56+) that predominate in decidua (83), and CD66a is upregulated in activated T-cells (83). Finally, CD66e expression by tumor cells is correlated with resistance to NK/LAK cell mediated lysis (64, 84). Thus, these data suggest that soluble CD66 family members could contribute to the immunosuppression often found in patients with cancer.

The biological activity of the peptides identified here suggests that they may have sufficient affinity to make them potential candidates for drug localization to cells expressing the appropriate surface structures.

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SEQUENCE FREE TEXT

SEQ ID NO:1-861 Synthetic Peptides

The complete disclosure of all patents, patent documents, and publications cited herein are incorporated by reference. The foregoing detailed description and examples have been given for clarity of understanding only. No unnecessary limitations are to be understood therefrom. The invention is not limited to the exact details shown and described, for variations obvious to one skilled in the art will be included within the invention defined by the claims.

WHAT IS CLAIMED IS:

1. An isolated peptide from a surface exposed region of a CD66 family member which is capable of modulating at least one of the following:

activation of neutrophils;

activation or inhibition of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells;

proliferation and/or differentiation of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells;

proliferation and/or differentiation of epithelial cells;

homotypic and/or heterotypic adhesion among CD66 family members; and adhesion of CD66 family members to other ligands.

2. A peptide of claim 1 consisting of an amino acid sequence selected from the group consisting of SEQ ID NO: 2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN,

SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; and analogs thereof that modulate the function of at least one CD66 family member and/or at least one ligand thereof.

3. The peptide of claim 1 which is complexed with a carrier molecule or structure to form a peptide conjugate.

4. The peptide conjugate of claim 3 wherein the carrier molecule or structure is selected from the group of microbeads, liposomes, biological carrier molecules, synthetic polymers, biomaterials, and cells.

5. The peptide conjugate of claim 3 wherein the peptide conjugate binds to cells expressing a CD66 protein or a CD66 ligand.

6. The peptide conjugate of claim 3 wherein the peptide conjugate includes a label.

7. The peptide of claim 1 which is attached to a label.

8. The peptide of claim 7 wherein the label is selected from the group consisting of a fluorescent tag, a radioactive tag, a magnetic resonance tag, an enzymatic tag, and combinations thereof.

9. A method of activating a neutrophil comprising contacting the neutrophil with at least one peptide of claim 1, a peptide conjugate thereof or analog thereof.

10. The method of claim 9 wherein the peptide is selected from the group consisting of SEQ ID NO:2-111 and 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF,

FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or a peptide conjugate thereof or analog thereof.

11. The method of claim 9 which is carried out *in vitro*.

12. The method of claim 9 which is carried out *in vivo*.

13. A method of blocking the activation of a neutrophil comprising contacting a neutrophil induced by the method of claim 9 with at least one peptide selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN,

FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or a peptide conjugate or analog thereof.

14. The method of claim 13 which is carried out *in vitro*.

15. The method of claim 13 which is carried out *in vivo*.

16. A method of modulating the homotypic and/or heterotypic adhesion of CD66 family members or adhesion of a CD66 protein to a CD66 ligand; the method comprising contacting CD66 family members and/or their ligands with at least one peptide selected from claim 1, a peptide conjugate or analog thereof.

17. The method of claim 16 wherein the peptide is selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG.

18. The method of claim 16 which is carried out *in vitro*.

19. The method of claim 16 which is carried out *in vivo*.

20. A method of altering the modulation of the homotypic and/or heterotypic adhesion of CD66 family members or adhesion between a CD66 protein and a CD66 ligand, the method comprising contacting the CD66 family

member and/or ligand of claim 16 with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or a peptide conjugate thereof or analog thereof.

21. The method of claim 20 which is carried out *in vitro*.

22. The method of claim 20 which is carried out *in vivo*.

23. A method of modulating immune cell activation, proliferation, and/or differentiation; the method comprising contacting an immune cell with at least one peptide or peptide conjugate of claim 1.

24. The method of claim 23 wherein the peptide is selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or an analog thereof.

25. The method of claim 23 wherein the immune cell is selected from the group of a T-cell, a B-cell, a LAK cell, an NK cell, a dendritic cell, and combinations thereof.

26. The method of claim 23 which is carried out *in vitro*.

27. The method of claim 23 which is carried out *in vivo*.

28. A method of modulating at least one of the following functions of CD66 family members and/or ligands thereof in cells: activation of neutrophils; activation or inhibition of T-cells, B-cells, NK cells, LAK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of T-cells, B-cells, LAK cells, NK cells, dendritic cells, or other immune system cells; proliferation and/or differentiation of epithelial cells; homotypic and/or heterotypic adhesion among CD66 family members; and adhesion of CD66 family members to other ligands; the method comprising contacting cells with at least one peptide of claim 1, a peptide conjugate thereof or an analog thereof.

29. A method of delivering a therapeutically active agent to a patient comprising administering at least one peptide conjugate to a patient, said peptide conjugate comprising a peptide and a therapeutically active agent and said peptide is selected form the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS,

SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG.

30. The method of claim 29 wherein the therapeutically active agent is selected from drugs, DNA sequences, RNA sequences, proteins, lipids, and combinations thereof.

31. The method of claim 29 wherein the therapeutically active agent is an antibacterial agent, antiinflammatory agent, or antineoplastic agent.

32. A method of modifying the metastasis of malignant cells comprising contacting the malignant cells or normal host tissue with at least one peptide or peptide conjugate, said peptide selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT,

TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

33. A method of altering bacterial or viral binding to cells or a biomaterial, the method comprising contacting the cells or biomaterial with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN,

SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

34. A method of altering cell adhesion to a biomaterial, the method comprising contacting the biomaterial with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

35. A method of detecting tumors comprising contacting tumor cells or tumor vasculature with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

36. A method of detecting inflammation comprising contacting inflamed vasculature or leukocytes with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE,

AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

37. A method of detecting a CD66 protein or a ligand thereof, the method comprising contacting tissue comprising a CD66 protein or a ligand thereof with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG,

TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT; VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

38. A method of altering angiogenesis comprising contacting endothelial cells, tumor cells, or immune cells with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN,

NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

39. A method of altering an immune response, the method comprising contacting immune system cells with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL,

VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

40. A method of altering keratinocyte proliferation comprising contacting keratinocytes with at least one peptide or peptide conjugate selected from the group consisting of SEQ ID NO:2-111, 135-861, TND, NDT, DTG, TGI, GIS, ISI, SIR, IRW, RWF, WFF, FFK, FKN, TN, ND, DT, TG, GI, IS, SI, IR, RW, WF, FF, FK, KN, STN, KNQ, SMP, MPF, PFN, FNV, NVA, VAE, AEG, EGK, GKE, KEV, EVL, SM, MP, PF, FN, NV, VA, AE, EG, GK, KE, EV, VL, LVH, VHN, HNL, NLP, LPQ, PQQ, QQL, QLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QQ, QL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QIV, IVG, VGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, IV, VG, VIK, IKS, KSD, SDL, DLV, LVN, VNE, NEE, EEA, EAT, ATG, TGQ, VI, IK, KS, SD, DL, LV, VN, NE, EE, EA, AT, TG, GQ, DPV, PVT, VTL, TLN, LNV, NVT, VTY, TYG, YGP, GPD, GPD, PDT, DP, PV, VT, TL, LN, NV, VT, TY,YG, GP, PD, DT, FIP, IPN, PNI, NIT, ITV, TVN, VNN, NNS, NSG, SGS, GSY, SYT, FI, IP, PN, NI, IT, TV, VN, NN, NS, SG, GS, SY, YT, TIY, IYP, YPN, PNA, NAS, ASL, SLL, LLI, LIQ, IQN, QNV, NVT,TI, IY, YP, PN, NA, AS, SL, LL, LI, IQ, QN, NV, VT, LVH, VHN, HNL, NLP, LPQ, PQH, QHL, HLF, LFG, FGY, GYS, YSW, LV, VH, HN, NL, LP, PQ, QH, HL, LF, FG, GY, YS, SW, KGE, GER, ERV, RVD, VDG, DGN, GNR, NRQ, RQI, QII, IIG, IGY, KG, GE, ER, RV, VD, DG, GN, NR, RQ, QI, II, IG, AAS, ASN, SNP, NPP, PPA, PAQ, AQY, QYS, YSW, SWF, WFV, FVN, AA, AS, SN, NP, PP, PA, AQ, QY, YS, SW, WF, FV, VN, SVD, VDH, DHS, HSD, SDP, DPV, PVI, VIL, ILN, LNV, NVL, VLY, SV, VD, DH, HS, SD, DP, PV, VI, IL, LN, NV, VL, LY, PEA, EAQ, AQN, QNT, NTT, TTY, TYL, YLW, LWW, WWV, WVN, VNG, PE, EA, AQ, QN, NT, TT,TY, YL, LW, WW, WV, VN and NG; or analogs thereof.

FIG. 1

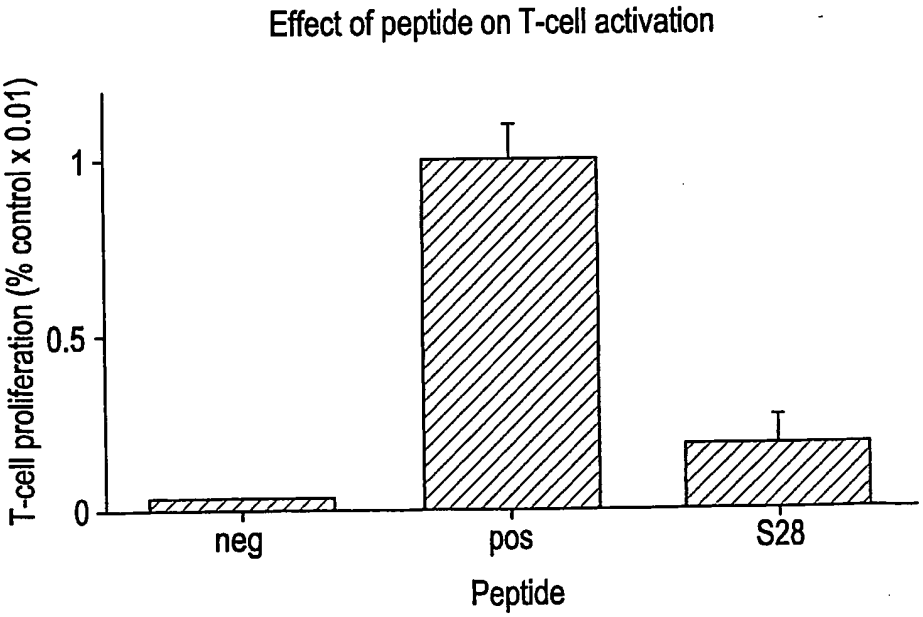

Effect of peptide on T-cell activation
T-cell proliferation (% control x 0.01)
1
0.5
0
neg
pos
S28
Peptide

FIG. 2

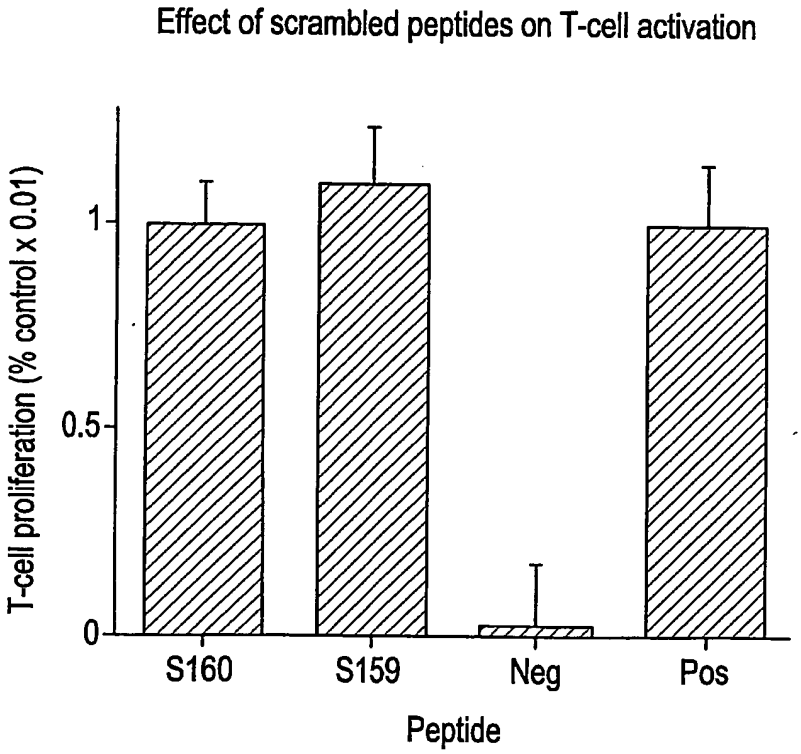
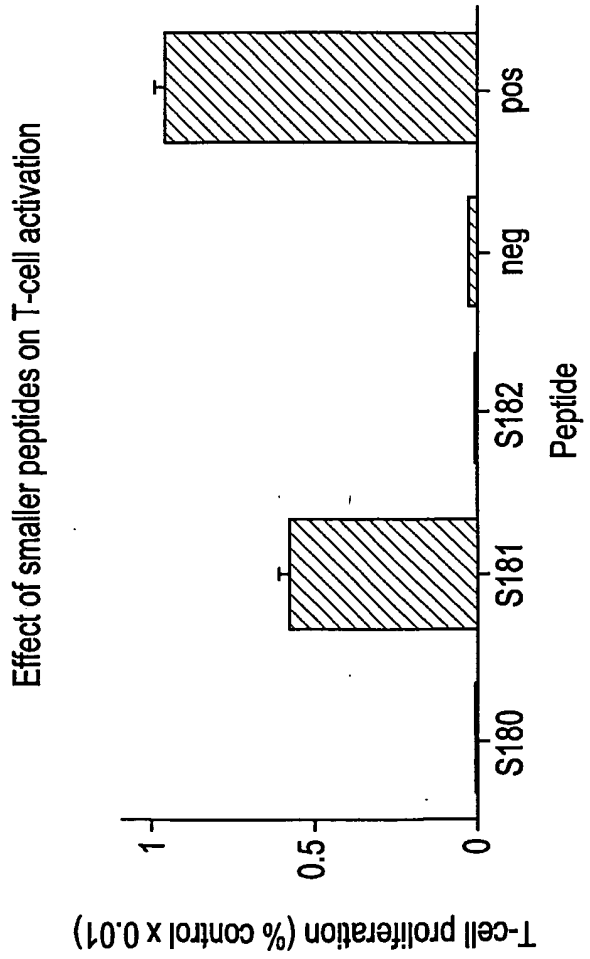

Effect of scrambled peptides on T-cell activation
T-cell proliferation (% control x 0.01)
1
0.5
0
S160
S159
Neg
Pos
Peptide

FIG. 3


Effect of smaller peptides on T-cell activation
T-cell proliferation (% control x 0.01)
0
0.5
1
S180
S181
S182
neg
pos
Peptide